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(71) Applicant: MERCK & CO. INC.
126, East Lincoln Avenue P.O. Box 2000
Rahway New Jersey 07065(US)

(72) Inventor: Ellis, Ronald W.
1407 Edgevale Road
Overbrook Hills Pennsylvania 19151(US)

(72) Inventor: Keller, Paul M.
2057 Spring Valley Road
Lansdale Pennsylvania 19446(US)

(74) Representative: Ahner, Francis et al,
CABINET REGIMBEAU 26, avenue Kléber
F-75116 Paris(FR)

(54) DNA sequences from Varicella-zoster virus, vectors and hosts containing them, the corresponding polypeptides and the compositions containing them.

(57) A gene of varicella-zoster virus (VZV) which encodes immunogenic outer surface viral proteins has been identified through DNA sequence analysis. Fragments of the DNA have been cloned into a vector which, when placed into a host organism, expresses proteins which react with human convalescent zoster sera and with monoclonal antibodies which neutralize viral infectivity. These proteins are useful for preparation of a vaccine for VZV.

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DNA SEQUENCE OF VARICELLA-ZOSTER VIRUS AND THEIR FRAGMENTS, THE VECTORS CONTAINING THEM, THE HOST CONTAINING THESE VECTORS, THE CORRESPONDING POLYPEPTIDES AND THE COMPOSITIONS CONTAINING THEM

BACKGROUND OF THE INVENTION

Chickenpox is caused by varicella-zoster virus (VZV), a member of the herpesvirus group. The disease occurs in persons with no prior VZV immunity. VZV-specific antibodies can be demonstrated shortly after onset of disease, decline during convalesence, but remain detectable for many years and correlate with immunity to the disease. Chickenpox is highly contagious; over 90% of the population becomes exposed to VZV during the first two decades. The disease is highly morbid to the immunosuppressed and to those beyond the second decade. In most, if not all cases, VZV becomes latent in dorsal root ganglion cells. From this latent state, VZV can reactivate and cause zoster even in the presence of specific antibodies, probably as a result of weakened cellular immunity.

VZV has six major glycoproteins on its surface: gp105, gp92, gp83, gp62, gp57, gp55. These glycoproteins apparently are the products of three genes: gA (gp105), gB (gp62, gp57) and gC (gp92, gp83, gp55). The gC glycoproteins are the majority and most immunogenic VZV glycoproteins. Some monoclonal antibodies to gA and gB display complement - independent neutralization, and monoclonal antibodies to gC display complement-dependent neutralization.

OBJECTS OF THE INVENTION

It is an object of the present invention to provide antigens which will prevent diseases associated with VZV infections. Another object is to provide antigens which can be used diagnostically to measure VZV antibody titers. Another object is to provide methods for the preparation of these antigens. Another object is to provide methods for using the antigens to raise antibodies, both in vivo and in vitro to VZV. Another object is to describe the full sequence of protein antigens which will include peptide antigens which may be synthesized by other means or expressed in other vectors. These and other objects of the present invention will be apparent from the following description.

SUMMARY OF THE INVENTION

The DNA sequence of the VZV gC gene has been identified. A fragment of the DNA has been cloned into a vector which, when placed in a host organism, expresses proteins which react with convalescent zoster sera and with neutralizing monoclonal antibodies to gC. These proteins are useful for preparation of a vaccine to VZV.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to identification of the VZV DNA which encodes the protective immunogenic glycoproteins gp92, gp83 and gp55. More specifically, it is directed to a 2.0 Kbp DNA fragment and to a 0.9 Kbp DNA fragment whose respective nucleotide sequences and amino acid sequences have been located within the known sequence of the entire VZV genome.

The present invention also is directed to vectors containing all or part of these 2.0 and 0.9 Kbp DNA fragments. The invention also is directed to host cells which contain these vectors and which cells are capable of expressing all or part of the peptides encoded by the 2.0 and 0.9 Kbp fragments. In accordance with known techniques, it will be obvious to those skilled in the art that parts of the foregoing peptides could be chemically synthesized or modified and retain their immunogenicity. Therefore, the present invention also is directed toward chemical synthesis of domains of these proteins, especially domains including and surrounding hydrophilic regions and threonine or serine and asparagine-X-serine or asparagine X-threonine residues (wherein X is any amino acid), since these domains are likely to reside on the outer surface of the virus.

RNAs are isolated from cells producing VZV. These RNAs are preselected by hybridization to the HindIII-C, EcoRI-A, or EcoRI-E DNA fragments and translated in vitro. The polypeptide products are immunoprecipitated with monoclonal antibody specific for gC polypeptides. These DNA fragments select RNA which translates to the 70Kd precursor of the gp92, gp83 and gp55 gC neutralizing antigens.

The DNA segment which encodes RNA translatable to gC polypeptides is identified precisely as follows. VZV DNA is randomly digested and 0.3-1.5 Kbp fragments are inserted into the pORF2 expression vector. Bacteria transformed by the recombinant plasmids are screened with monoclonal antibodies for the production of gC antigens. Plasmid DNA from E. coli expressing gC antigens is hybridized to restriction fragments of VZV genomic DNA, and homology is identified within the HindIII-C fragment. DNA sequence analysis of the VZV DNA within the expression plasmid reveals identity to a 0.9 Kbp segment within the HindIII-C fragment whose DNA sequence is known. This 0.9 Kbp segment is part of a single long 2.0 Kbp open reading frame whose DNA sequence is known and which encodes a 70Kd immunogenic protein.

The hybrid protein containing VZV gC sequences derived from the 0.9 Kbp DNA segment is characterized with respect to serological reactivity. It is found to react with 8 of 11 convalescent zoster sera tested as well as with 7 of 8 neutralizing monoclonal antibodies to VZV gC. Therefore, this polypeptide segment carries neutralization epitopes as well as the majority of antigenicity associated with gC polypeptides.

Examples of suitable hosts for expression of VZV proteins include prokaryotic organisms, such as E. coli and B. subtilis, and eukaryotic organisms such as S. cerevisiae and continuous mammalian cell lines including Chinese Hamster ovary cells and diploid mammalian fibroblasts such as WI-38 and MRC-5 cells.

These proteins are usefully individually or in combination when placed in a physiologically acceptable carrier, e.g., saline or phosphate buffered saline, to protect against VZV disease when administered to a member of a susceptible mammalian species in amount of approximately 10 to 500 µg per dose, preferably from approximately 50 to 250 µg per dose. One or more doses may be administered to produce effective protection against VZV disease. The protein may be administered by injection, e.g., subcutaneously or intramuscularly. It is also to be understood that these proteins can be directly expressed in humans by means of appropriate viral expression vectors such as adeno, vaccinia, or herpes simplex.

The following examples illustrate the present invention without, however, limiting the same thereto. The disclosure of each reference mentioned in the following examples is hereby incorporated by reference.

EXAMPLE 1

DNA Fragments Which Select RNA Encoding the Precursor Protein to gC glycoproteins

Cytoplasmic polyadenylated RNAs were prepared from VZV-infected MRC-5 cells as described (Biochemistry 18: 5294-5299, 1979). The RNAs encoded by the VZV DNA HindIII-C, EcoRI-A and EcoRI-E fragments were selected by hybridization to cloned VZV DNA (Proc. Natl. Acad. Sci. 79: 156-160, 1982) bound to nitrocellulose (J. Virology 37: 284-294, 1981). These RNAs were translated in a rabbit reticulocyte lysate as previously described (Evr. J. Biochem. 67: 247-254, 1976). The polypeptide

products were immunoprecipitated with neutralizing monoclonal antibodies specific for VZV gC (J. Virology in press, 1984) and with convalescent zoster serum, as previously described (J. Virology in press, 1984). These DNA fragments select RNAs which include that which translates to the 70Kd gC precursor (Virology 129: 357-368, 1983).

EXAMPLE 2

Determination of the VZV DNA sequence which encodes gC antigens

A library of VZV DNA clones (Proc. Natl. Acad. Sci. 79: 156-160, 1982) was randomly digested by DNaseI in the presence of Mn^{++} (Nucleic Acids Research 9: 3015-3027, 1981) in order to produce DNA in the size range of 0.1-2.5 Kbp. From this pool, DNA sized 0.3-1.5 Kbp was purified, made flush-ended, and cloned into the SmaI site of the pORF2 expression vector (Proc. Natl. Acad. Sci. 80: 4432-4436, 1983). The recombinant plasmids were introduced into E. coli TK1046 (1048). Bacterial colonies expressing hybrid proteins containing VZV polypeptides were selected, and such colonies were screened with monoclonal antibodies for the expression of VZV gC antigens. A colony expressing a VZV gC hybrid protein was isolated. The VZV antigens were recognized by 7 of 8 monoclonal antibodies to gC and by 8 of 11 convalescent zoster sera. The plasmid DNA from this colony was isolated and hybridized to restriction endonuclease digests of VZV genomic DNA (J. Mol. Biol. 98: 503-521, 1975). In this manner, the VZV insert in the bacterial plasmid was shown to be homologous to a 0.9 Kbp DNA sequence in the HindIII-C

DNA clone. This segment of HindIII-C DNA, therefore, was identified as a part of the gC gene.

EXAMPLE 3

Determination of Nucleotide Sequences of the 0.9 and 2.0 Kbp segments of VZV DNA

The complete nucleotide sequence of the VZV HindIII-C DNA segment contains several large open reading frames (EMBO Journal 2: 2203-2209, 1983). One of these open reading frames is 2.0 Kbp in length, encodes a 70 Kd protein, and contains within it that 0.9 Kbp segment described in Example 2 which encodes VZV gC antigens.

A. The nucleotide sequence for the complete 2.0 Kbp segment which encodes the gC glycoprotein is given below:

ATG TTT TAT GAA GCC TTA AAG GCC GAG CTG GTA TAC ACG
AGA GCA GTC CAT GGT TTT AGA CCT CGG GCG AAT TGC GTG
GTT TTA AGT GAC TAT ATT CCG AGG GTC GCC TGT AAT ATG
GGG ACA GTT AAT AAA CCT GTG GTG GGG GTA TTG ATG GGG
TTC GGA ATT ATC ACG GGA ACG TTG CGT ATA ACG AAT CCG
GTC AGA GCA TCC GTC TTG CGA TAC GAT GAT TTT CAC ACC
GAT GAA GAC AAA CTG GAT ACA AAC TCC GTA TAT GAG CCT
TAC TAC CAT TCA GAT CAT GCG GAG TCT TCA TGG GTA AAT
CGG GGA GAG TCT TCG CGA AAA GCG TAC GAT CAT AAC TCA
CCT TAT ATA TGG CCA CGT AAT GAT TAT GAT GGA TTT TTA
GAG AAC GCA CAC GAA CAC CAT GGG GTG TAT AAT CAG GGC
CGT GGT ATC GAT AGC GGG GAA CGG TTA ATG CAA CCC ACA
CAA ATG TCT GCA CAG GAG GAT CTT GGG GAC GAT ACG GGC
ATC CAC GTT ATC CCT ACG TTA AAC GGC GAT GAC AGA CAT

AAA ATT GTA AAT GTG GAC CAA CGT CAA TAC GGT GAC GTG
TTT AAA GGA GAT CTT AAT CCA AAA CCC CAA GGC CAA AGA
CTC ATT GAG GTG TCA GTG GAA GAA AAT CAC CCG TTT ACT
TTA CGC GCA CCG ATT CAG CGG ATT TAT GGA GTC CGG TAC
ACC GAG ACT TGG AGC TTT TTG CCG TCA TTA ACC TGT ACG
GGA GAC GCA GCG CCC GCC ATC CAG CAT ATA TGT TTA AAA
CAT ACA ACA TGC TTT CAA GAC GTG GTG GTG GAT GTG GAT
TGC GCG GAA AAT ACT AAA GAG GAT CAG TTG GCC GAA ATC
AGT TAC CGT TTT CAA GGT AAG AAG GAA GCG GAC CAA CCG
TGG ATT GTT GTA AAC ACG AGC ACA CTG TTT GAT GAA CTC
GAA TTA GAC CCC CCC GAG ATT GAA CCG GGT GTC TTG AAA
GTA CTT CGG ACA GAA AAA CAA TAC TTG GGT GTG TAC ATT
TGG AAC ATG CGC GGC TCC GAT GGT ACG TCT ACC TAC GCC
ACG TTT TTG GTC ACC TGG AAA GGG GAT GAA AAA ACA AGA
AAC CCT ACG CCC GCA GTA ACT CCT CAA CCA AGA GGG GCT
GAG TTT CAT ATG TGG AAT TAC CAC TCG CAT GTA TTT TCA
GTT GGT GAT ACG TTT AGC TTG GCA ATG CAT CTT CAG TAT
AAG ATA CAT GAA GCG CCA TTT GAT TTG CTG TTA GAG TGG
TTG TAT GTC CCC ATC GAT CCT ACA TGT CAA CCA ATG CGG
TTA TAT TCT ACG TGT TTG TAT CAT CCC AAC GCA CCC CAA
TGC CTC TCT CAT ATG AAT TCC GGT TGT ACA TTT ACC TCG
CCA CAT TTA GCC CAG CGT GTT GCA AGC ACA GTG TAT CAA
AAT TGT GAA CAT GCA GAT AAC TAC ACC GCA TAT TGT CTG
GGA ATA TCT CAT ATG GAG CCT AGC TTT GGT CTA ATC TTA
CAC GAC GGG GGC ACC ACG TTA AAG TTT GTA GAT ACA CCC
GAG AGT TTG TCG GGA TTA TAC GTT TTT GTG GTG TAT TTT
AAC GGG CAT GTT GAA GCC GTA GCA TAC ACT GTT GTA TCC
ACA GTA GAT CAT TTT GTA AAC GCA ATT GAA GAG CGT GGA
TTT CCG CCA ACG GCC GGT CAG CCA CCG GCG ACT ACT AAA
CCC AAG GAA ATT ACC CCC GTA AAC CCC GGA ACG TCA CCA
CTT CTA CGA TAT GCC GCA TGG ACC GGA GGG CTT GCA GCA
GTA GTA CTT TTA TGT CTC GTA ATA TTT TTA ATC TGT ACG

GCT AAA CGA ATG AGG GTT AAA GCC TAT AGG GTA GAC AAG
TCC CCG TAT AAC CAA AGC ATG TAT TAC GCT GGC CTT CCA
GTG GAC GAT TTC GAG GAC TCG GAA TCT ACG GAT ACG GAA
GAA GAG TTT GGT AAC GCG ATT GGA GGG AGT CAC GGG GGT
TCG AGT TAC ACG GTG TAT ATA GAT AAG ACC CGG TGA

The foregoing nucleotide sequence codes for the following amino acid sequence:

M	F	Y	E	A	L	K	A	E	L
V	Y	T	R	A	V	H	G	F	R
P	R	A	N	C	V	V	L	S	D
Y	I	P	R	V	A	C	N	M	G
T	V	N	K	P	V	V	G	V	L
M	G	F	G	I	I	T	G	T	L
R	I	T	N	P	V	R	A	S	V
L	R	Y	D	D	F	H	T	D	E
D	K	L	D	T	N	S	V	Y	E
P	Y	Y	H	S	D	H	A	E	S
S	W	V	N	R	G	E	S	S	R
K	A	Y	D	H	N	S	P	Y	I
W	P	R	N	D	Y	D	G	F	L
E	N	A	H	E	H	H	G	V	Y
N	Q	G	R	G	I	D	S	G	E
R	L	M	Q	P	T	Q	M	S	A
Q	E	D	L	G	D	D	T	G	I
H	V	I	P	T	L	N	G	D	D
R	H	K	I	V	N	V	D	Q	R
Q	Y	G	D	V	F	K	G	D	L
N	P	K	P	Q	G	Q	R	L	I
E	V	S	V	E	E	N	H	P	F
T	L	R	A	P	I	Q	R	I	Y
G	V	R	Y	T	E	T	W	S	F

	L	P	S	L	T	C	T	G	D	A
	A	P	A	I	Q	H	I	C	L	K
	H	T	T	C	F	Q	D	V	V	V
	D	V	D	C	A	E	N	T	K	E
5	D	Q	L	A	E	I	S	Y	R	F
	Q	G	K	K	E	A	D	Q	P	W
	I	V	V	N	T	S	T	L	F	D
	E	L	E	L	D	P	P	E	I	E
	P	G	V	L	K	V	L	R	T	E
10	K	Q	Y	L	G	V	Y	I	W	N
	M	R	G	S	D	G	T	S	T	Y
	A	T	F	L	V	T	W	K	G	D
	E	K	T	R	N	P	T	P	A	V
	T	P	Q	P	R	G	A	E	F	H
15	M	W	N	Y	H	S	H	V	F	S
	V	G	D	T	F	S	L	A	M	H
	L	Q	Y	K	I	H	E	A	P	F
	D	L	L	L	E	W	L	Y	V	P
	I	D	P	T	C	Q	P	M	R	L
20	Y	S	T	C	L	Y	H	P	N	A
	P	Q	C	L	S	H	M	N	S	G
	C	T	F	T	S	P	H	L	A	Q
	R	V	A	S	T	V	Y	Q	N	C
	E	H	A	D	N	Y	T	A	Y	C
25	L	G	I	S	H	M	E	P	S	F
	G	L	I	L	H	D	G	G	T	T
	L	K	F	V	D	T	P	E	S	L
	S	G	L	Y	V	F	V	V	Y	F
	N	G	H	V	E	A	V	A	Y	T
30	V	V	S	T	V	D	H	F	V	N
	A	I	E	E	R	G	F	P	P	T
	A	G	Q	P	P	A	T	T	K	P
	K	E	I	T	P	V	N	P	G	T

S P L L R Y A A W T
G G L A A V V L L C
L V I F L I C T A K
R M R V K A Y R V D
K S P Y N Q S M Y Y
A G L P V D D F E D
S E S T D T E E E F
G N A I G G S H G G
S S Y T V Y I D K T
R

In the foregoing and succeeding sequences the letters represent the following amino acids:

A	Ala	Alanine
C	Cys	Cysteine
D	Asp	Aspartic acid
E	Glu	Glutamic acid
F	Phe	Phenylalanine
G	Gly	Glycine
H	His	Histidine
I	Ile	Isoleucine
K	Lys	Lysine
L	Leu	Leucine
M	Met	Methionine
N	Asn	Asparagine
P	Pro	Proline
Q	Gln	Glutamine
R	Arg	Arginine
S	Ser	Serine
T	Thr	Threonine
V	Val	Valine
W	Trp	Tryptophan
Y	Tyr	Tyrosine

B. The nucleotide sequence for 60 bases at each terminus of the 0.9 Kbp segment was determined and aligned with the published 6.2 Kbp DNA sequence. The 0.9 DNA sequence and the 35 Kd gC protein segment, which encodes virtually all the major antigenicity of gC as well as neutralization epitopes, is given below:

TTT CAC ACC GAT GAA GAC AAA CTG GAT ACA AAC TCC GTA
TAT GAG CCT TAC TAC CAT TCA GAT CAT GCG GAG TCT TCA
TGG GTA AAT CGG GGA GAG TCT TCG CGA AAA GCG TAC GAT
CAT AAC TCA CCT TAT ATA TGG CCA CGT AAT GAT TAT GAT
GGA TTT TTA GAG AAC GCA CAC GAA CAC CAT GGG GTG TAT
AAT CAG GGC CGT GGT ATC GAT AGC GGG GAA CGG TTA ATG
CAA CCC ACA CAA ATG TCT GCA CAG GAG GAT CTT GGG GAC
GAT ACG GGC ATC CAC GTT ATC CCT ACG TTA AAC GGC GAT
GAC AGA CAT AAA ATT GTA AAT GTG GAC CAA CGT CAA TAC
GGT GAC GTG TTT AAA GGA GAT CTT AAT CCA AAA CCC CAA
GGC CAA AGA CTC ATT GAG GTG TCA GTG GAA GAA AAT CAC
CCG TTT ACT TTA CGC GCA CCG ATT CAG CGG ATT TAT GGA
GTC CGG TAC ACC GAG ACT TGG AGC TTT TTG CCG TCA TTA
ACC TGT ACG GGA GAC GCA GCG CCC GCC ATC CAG CAT ATA
TGT TTA AAA CAT ACA ACA TGC TTT CAA GAC GTG GTG GTG
GAT GTG GAT TGC GCG GAA AAT ACT AAA GAG GAT CAG TTG
GCC GAA ATC AGT TAC CGT TTT CAA GGT AAG AAG GAA GCG
GAC CAA CCG TGG ATT GTT GTA AAC ACG AGC ACA CTG TTT
GAT GAA CTC GAA TTA GAC CCC CCC GAG ATT GAA CCG GGT
GTC TTG AAA GTA CTT CGG ACA GAA AAA CAA TAC TTG GGT
GTG TAC ATT TGG AAC ATG CGC GGC TCC GAT GGT ACG TCT
ACC TAC GCC ACG TTT TTG GTC ACC TGG AAA GGG GAT GAA
AAA ACA AGA AAC CCT ACG CCC GCA GTA ACT CCT CAA CCA
AGA

The foregoing nucleotide sequence codes for the following amino acid sequence:

	F	H	T	D	E	D	K	L	D	T
5	N	S	V	Y	E	P	Y	Y	H	S
	D	H	A	E	S	S	W	V	N	R
	G	E	S	S	R	K	A	Y	D	H
	N	S	P	Y	I	W	P	R	N	D
	Y	D	G	F	L	E	N	A	H	E
10	H	H	G	V	Y	N	Q	G	R	G
	I	D	S	G	E	R	L	M	Q	P
	T	Q	M	S	A	Q	E	D	L	G
	D	D	T	G	I	H	V	I	P	T
	L	N	G	D	D	R	H	K	I	V
15	N	V	D	Q	R	Q	Y	G	D	V
	F	K	G	D	L	N	P	K	P	Q
	G	Q	R	L	I	E	V	S	V	E
	E	N	H	P	F	T	L	R	A	P
	I	Q	R	I	Y	G	V	R	Y	T
20	E	T	W	S	F	L	P	S	L	T
	C	T	G	D	A	A	P	A	I	Q
	H	I	C	L	K	H	T	T	C	F
	Q	D	V	V	V	D	V	D	C	A
	E	N	T	K	E	D	Q	L	A	E
25	I	S	Y	R	F	Q	G	K	K	E
	A	D	Q	P	W	I	V	V	N	T
	S	T	L	F	D	E	L	E	L	D
	P	P	E	I	E	P	G	V	L	K
	V	L	R	T	E	K	Q	Y	L	G
30	V	Y	I	W	N	M	R	G	S	D
	G	T	S	T	Y	A	T	F	L	V
	T	W	K	G	D	E	K	T	R	N
	P	T	P	A	V	T	P	Q	P	R

Either of the foregoing peptides may be formulated into a vaccine by admixing with a physiologically acceptable carrier and administering parenterally to susceptible mammalian species to induce formation of protective, including neutralizing, antibodies. The dosage level may be from about 5 to about 200 ug in from about one to about 3 doses.

EXAMPLE 4

Purified VZV viral gC polypeptide induces antibodies which neutralize VZV infectivity in vitro

VZV gC glycoprotein was purified from MRC-5 cells by means of immuno-affinity chromatography utilizing monoclonal antibodies to VZV gC as described in Keller et al., J. Virol., 52:293-297, 1984. Analysis of this purified glycoprotein by silver staining of sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) resolution demonstrated essentially homogeneous VZV gC with the same molecular weight as described in Keller et al. (ibid.). Guinea pigs were inoculated intramuscularly with 20 micrograms of VZV gC in complete Freund's adjuvant, followed one month later by two inoculations each of ten micrograms of VZV gC in incomplete Freund's adjuvant spaced two weeks apart. Sera were obtained from the guinea pigs before and after inoculation. Each of the guinea pig sera were utilized in an in vitro VZV neutralization assay as described (Keller et al., ibid.). By this assay the post-immunization but not the pre-immunization sera elicited VZV neutralizing antibodies.

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EXAMPLE 5

Recombinant E. coli-derived gC polypeptide induces antibodies which neutralize VZV infectivity in vitro

. VZV gC protein was produced in E. coli as described by Ellis et al., J. Virol., 53:81-88, 1985. Forty micrograms of E. coli-derived VZV gC was adsorbed onto 5% alhydrogel in 0.15 M NaCl, .01 M Na_2HPO_4, pH 7.2. Six micrograms of VZV gC on alhydrogel was inoculated thrice intramuscularly into each of two guinea pigs at two-week intervals. Sera were taken before inoculation and two weeks after the last inoculation. Each of the guinea pig sera were utilized in an in vitro VZV neutralization assay as described (Keller et al.) J. Virol., 52:293-297, 1984. By this assy, the post-immunization but not the pre-immunization sera elicited VZV neutralizing antibodies. Therefore VZV gC is capable of eliciting virus neutralizing antibodies.

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WHAT IS CLAIMED IS:

1. A DNA segment which codes for at least part of VZV glycoprotein C.

2. A 2.0 Kbp fragment of VZV DNA of Claim 1 having the nucleotide sequence:

ATG TTT TAT GAA GCC TTA AAG GCC GAG CTG GTA TAC ACG
AGA GCA GTC CAT GGT TTT AGA CCT CGG GCG AAT TGC GTG
GTT TTA AGT GAC TAT ATT CCG AGG GTC GCC TGT AAT ATG
GGG ACA GTT AAT AAA CCT GTG GTG GGG GTA TTG ATG GGG
TTC GGA ATT ATC ACG GGA ACG TTG CGT ATA ACG AAT CCG
GTC AGA GCA TCC GTC TTG CGA TAC GAT GAT TTT CAC ACC
GAT GAA GAC AAA CTG GAT ACA AAC TCC GTA TAT GAG CCT
TAC TAC CAT TCA GAT CAT GCG GAG TCT TCA TGG GTA AAT
CGG GGA GAG TCT TCG CGA AAA GCG TAC GAT CAT AAC TCA
CCT TAT ATA TGG CCA CGT AAT GAT TAT GAT GGA TTT TTA
GAG AAC GCA CAC GAA CAC CAT GGG GTG TAT AAT CAG GGC
CGT GGT ATC GAT AGC GGG GAA CGG TTA ATG CAA CCC ACA
CAA ATG TCT GCA CAG GAG GAT CTT GGG GAC GAT ACG GGC
ATC CAC GTT ATC CCT ACG TTA AAC GGC GAT GAC AGA CAT
AAA ATT GTA AAT GTG GAC CAA CGT CAA TAC GGT GAC GTG
TTT AAA GGA GAT CTT AAT CCA AAA CCC CAA GGC CAA AGA
CTC ATT GAG GTG TCA GTG GAA GAA AAT CAC CCG TTT ACT
TTA CGC GCA CCG ATT CAG CGG ATT TAT GGA GTC CGG TAC
ACC GAG ACT TGG AGC TTT TTG CCG TCA TTA ACC TGT ACG
GGA GAC GCA GCG CCC GCC ATC CAG CAT ATA TGT TTA AAA
CAT ACA ACA TGC TTT CAA GAC GTG GTG GTG GAT GTG GAT
TGC GCG GAA AAT ACT AAA GAG GAT CAG TTG GCC GAA ATC
AGT TAC CGT TTT CAA GGT AAG AAG GAA GCG GAC CAA CCG
TGG ATT GTT GTA AAC ACG AGC ACA CTG TTT GAT GAA CTC
GAA TTA GAC CCC CCC GAG ATT GAA CCG GGT GTC TTG AAA
GTA CTT CGG ACA GAA AAA CAA TAC TTG GGT GTG TAC ATT
TGG AAC ATG CGC GGC TCC GAT GGT ACG TCT ACC TAC GCC
ACG TTT TTG GTC ACC TGG AAA GGG GAT GAA AAA ACA AGA

AAC CCT ACG CCC GCA GTA ACT CCT CAA CCA AGA GGG GCT
GAG TTT CAT ATG TGG AAT TAC CAC TCG CAT GTA TTT TCA
GTT GGT GAT ACG TTT AGC TTG GCA ATG CAT CTT CAG TAT
AAG ATA CAT GAA GCG CCA TTT GAT TTG CTG TTA GAG TGG
TTG TAT GTC CCC ATC GAT CCT ACA TGT CAA CCA ATG CGG
TTA TAT TCT ACG TGT TTG TAT CAT CCC AAC GCA CCC CAA
TGC CTC TCT CAT ATG AAT TCC GGT TGT ACA TTT ACC TCG
CCA CAT TTA GCC CAG CGT GTT GCA AGC ACA GTG TAT CAA
AAT TGT GAA CAT GCA GAT AAC TAC ACC GCA TAT TGT CTG
GGA ATA TCT CAT ATG GAG CCT AGC TTT GGT CTA ATC TTA
CAC GAC GGG GGC ACC ACG TTA AAG TTT GTA GAT ACA CCC
GAG AGT TTG TCG GGA TTA TAC GTT TTT GTG GTG TAT TTT
AAC GGG CAT GTT GAA GCC GTA GCA TAC ACT GTT GTA TCC
ACA GTA GAT CAT TTT GTA AAC GCA ATT GAA GAG CGT GGA
TTT CCG CCA ACG GCC GGT CAG CCA CCG GCG ACT ACT AAA
CCC AAG GAA ATT ACC CCC GTA AAC CCC GGA ACG TCA CCA
CTT CTA CGA TAT GCC GCA TGG ACC GGA GGG CTT GCA GCA
GTA GTA CTT TTA TGT CTC GTA ATA TTT TTA ATC TGT ACG
GCT AAA CGA ATG AGG GTT AAA GCC TAT AGG GTA GAC AAG
TCC CCG TAT AAC CAA AGC ATG TAT TAC GCT GGC CTT CCA
GTG GAC GAT TTC GAG GAC TCG GAA TCT ACG GAT ACG GAA
GAA GAG TTT GGT AAC GCG ATT GGA GGG AGT CAC GGG GGT
TCG AGT TAC ACG GTG TAT ATA GAT AAG ACC CGG TGA

3. A 0.9 Kbp fragment of VZV DNA of Claim 1 having the nucleotide sequence:

TTT CAC ACC GAT GAA GAC AAA CTG GAT ACA AAC TCC GTA
TAT GAG CCT TAC TAC CAT TCA GAT CAT GCG GAG TCT TCA
TGG GTA AAT CGG GGA GAG TCT TCG CGA AAA GCG TAC GAT
CAT AAC TCA CCT TAT ATA TGG CCA CGT AAT GAT TAT GAT
GGA TTT TTA GAG AAC GCA CAC GAA CAC CAT GGG GTG TAT
AAT CAG GGC CGT GGT ATC GAT AGC GGG GAA CGG TTA ATG

CAA CCC ACA CAA ATG TCT GCA CAG GAG GAT CTT GGG GAC
GAT ACG GGC ATC CAC GTT ATC CCT ACG TTA AAC GGC GAT
GAC AGA CAT AAA ATT GTA AAT GTG GAC CAA CGT CAA TAC
GGT GAC GTG TTT AAA GGA GAT CTT AAT CCA AAA CCC CAA
GGC CAA AGA CTC ATT GAG GTG TCA GTG GAA GAA AAT CAC
CCG TTT ACT TTA CGC GCA CCG ATT CAG CGG ATT TAT GGA
GTC CGG TAC ACC GAG ACT TGG AGC TTT TTG CCG TCA TTA
ACC TGT ACG GGA GAC GCA GCG CCC GCC ATC CAG CAT ATA
TGT TTA AAA CAT ACA ACA TGC TTT CAA GAC GTG GTG GTG
GAT GTG GAT TGC GCG GAA AAT ACT AAA GAG GAT CAG TTG
GCC GAA ATC AGT TAC CGT TTT CAA GGT AAG AAG GAA GCG
GAC CAA CCG TGG ATT GTT GTA AAC ACG AGC ACA CTG TTT
GAT GAA CTC GAA TTA GAC CCC CCC GAG ATT GAA CCG GGT
GTC TTG AAA GTA CTT CGG ACA GAA AAA CAA TAC TTG GGT
GTG TAC ATT TGG AAC ATG CGC GGC TCC GAT GGT ACG TCT
ACC TAC GCC ACG TTT TTG GTC ACC TGG AAA GGG GAT GAA
AAA ACA AGA AAC CCT ACG CCC GCA GTA ACT CCT CAA CCA
AGA

4. A polypetide coded for by the DNA fragment of Claim 2 having the amino acid sequence:

M F Y E A L K A E L
V Y T R A V H G F R
P R A N C V V L S D
Y I P R V A C N M G
T V N K P V V G V L
M G F G I I T G T L
R I T N P V R A S V
L R Y D D F H T D E
D K L D T N S V Y E
P Y Y H S D H A E S
S W V N R G E S S R

	K	A	Y	D	H	N	S	P	Y	I
	W	P	R	N	D	Y	D	G	F	L
	E	N	A	H	E	H	H	G	V	Y
	N	Q	G	R	G	I	D	S	G	E
5	R	L	M	Q	P	T	Q	M	S	A
	Q	E	D	L	G	D	D	T	G	I
	H	V	I	P	T	L	N	G	D	D
	R	H	K	I	V	N	V	D	Q	R
	Q	Y	G	D	V	F	K	G	D	L
10	N	P	K	P	Q	G	Q	R	L	I
	E	V	S	V	E	E	N	H	P	F
	T	L	R	A	P	I	Q	R	I	Y
	G	V	R	Y	T	E	T	W	S	F
	L	P	S	L	T	C	T	G	D	A
15	A	P	A	I	Q	H	I	C	L	K
	H	T	T	C	F	Q	D	V	V	V
	D	V	D	C	A	E	N	T	K	E
	D	Q	L	A	E	I	S	Y	R	F
	Q	G	K	K	E	A	D	Q	P	W
20	I	V	V	N	T	S	T	L	F	D
	E	L	E	L	D	P	P	E	I	E
	P	G	V	L	K	V	L	R	T	E
	K	Q	Y	L	G	V	Y	I	W	N
	M	R	G	S	D	G	T	S	T	Y
25	A	T	F	L	V	T	W	K	G	D
	E	K	T	R	N	P	T	P	A	V
	T	P	Q	P	R	G	A	E	F	H
	M	W	N	Y	H	S	H	V	F	S
	V	G	D	T	F	S	L	A	M	H
3.	L	Q	Y	K	I	H	E	A	P	F
	D	L	L	L	E	W	L	Y	V	P
	I	D	P	T	C	Q	P	M	R	L
	Y	S	T	C	L	Y	H	P	N	A

P Q C L S H M N S G
C T F T S P H L A Q
R V A S T V Y Q N C
E H A D N Y T A Y C
L G I S H M E P S F
G L I L H D G G T T
L K F V D T P E S L
S G L Y V F V V Y F
N G H V E A V A Y T
V V S T V D H F V N
A I E E R G F P P T
A G Q P P A T T K P
K E I T P V N P G T
S P L L R Y A A W T
G G L A A V V L L C
L V I F L I C T A K
R M R V K A Y R V D
K S P Y N Q S M Y Y
A G L P V D D F E D
S E S T D T E E E F
G N A I G G S H G G
S S Y T V Y I D K T
R

5. A polypeptide coded for by the DNA fragment of Claim 3 having the amino acid sequence:

F H T D E D K L D T
N S V Y E P Y Y H S
D H A E S S W V N R
G E S S R K A Y D H
N S P Y I W P R N D
Y D G F L E N A H E

H	H	G	V	Y	N	Q	G	R	G
I	D	S	G	E	R	L	M	Q	P
T	Q	M	S	A	Q	E	D	L	G
D	D	T	G	I	H	V	I	P	T
L	N	G	D	D	R	H	K	I	V
N	V	D	Q	R	Q	Y	G	D	V
F	K	G	D	L	N	P	K	P	Q
G	Q	R	L	I	E	V	S	V	E
E	N	H	P	F	T	L	R	A	P
I	Q	R	I	Y	G	V	R	Y	T
E	T	W	S	F	L	P	S	L	T
C	T	G	D	A	A	P	A	I	Q
H	I	C	L	K	H	T	T	C	F
Q	D	V	V	V	D	V	D	C	A
E	N	T	K	E	D	Q	L	A	E
I	S	Y	R	F	Q	G	K	K	E
A	D	Q	P	W	I	V	V	N	T
S	T	L	F	D	E	L	E	L	D
P	P	E	I	E	P	G	V	L	K
V	L	R	T	E	K	Q	Y	L	G
V	Y	I	W	N	M	R	G	S	D
G	T	S	T	Y	A	T	F	L	V
T	W	K	G	D	E	K	T	R	N
P	T	P	A	V	T	P	Q	P	R

6. A recombinant DNA transfer vector comprising a transfer vector into which a DNA seqment of Claim 1 has been inserted.

7. A vector containing all or part of the 2.0 Kbp VZV DNA fragment of Claim 2, the vector adapted to express in a suitable host at least part of the protein of gC coded by the VZV DNA fragment.

8. A vector according to Claim 7, wherein the host is a prokaryotic or eukaryotic organism.

9. A vector containing all or part of the 0.9 Kbp VZV DNA fragment of Claim 3, the vector adapted to express in a suitable host at least part of the protein of gC encoded by the VZV DNA fragment.

10. A vector according to Claim 9 wherein the host is a prokaryotic or eukaryotic organism.

11. A suitable prokaryotic or eukaryotic host containing a vector according to Claim 7, the host adapted to express at least part of the protein of gC coded by the 2.0 Kbp VZV DNA fragment.

12. A suitable prokaryotic or eukaryotic host containing a vector according to Claim 9, the host adapted to express at least part of the protein of gC coded by the 0.9 Kbp VZV DNA fragment.

13. A composition comprising the polypeptide of Claim 4 or a subunit thereof in a suitable carrier.

14. A composition comprising the polypeptide of Claim 5 or a subunit thereof in a suitable carrier.

15. A viral expression vector according to Claim 7 wherein all or part of said protein is expressed directly in a mammalian species.

16. A viral expression vector according to Claim 9 wherein all or part of said protein is expressed directly in a mammalian species.